REMARKS/ARGUMENTS

I. Status of the claims

No claims are amended. Claims 15-17, 23-26, and 31-41 are pending.

II. Rejection under 35 U.S.C. § 103

The Examiner rejected claims 15-17, 23-26 and 31-41 as allegedly obvious in view of Lowe *et al.* in view of Wittwer *et al.* Specifically, the Examiner argued that Lowe *et al.* taught all of the steps of the claims aside from a step of determining a non-linear continuously differentiable function of a logarithm of copy number as a function of the cycle number at which the signal threshold value is exceeded (such as found in step (e) of claim 15). The Examiner also acknowledged that Lowe *et al.* did not describe detecting an amplified nucleic acid using a DNA-binding dye. The Examiner argued that Wittwer *et al.* described the steps omitted in Lowe *et al.* Applicants respectfully traverse the rejection.

To set forth a *prima facie* obviousness rejection, the combination of references must describe all of the claimed elements. In the present rejection, the cited reference do not include a description of determining a non-linear continuously differentiable function of a logarithm of copy number as a function of the cycle number at which the signal threshold value is exceeded, as recited, for example in step (e) of claim 15.

The present claims currently involve steps that include making a dilution series of target nucleic acids (e.g., step (a) of claim 15), amplifying the nucleic acids (step (b)), and determining a non-linear continuously differentiable function of a logarithm of copy number as a function of the cycle number at which the signal threshold value is exceeded (step (e)). The determination of a non-linear function involves plotting the logarithm of the initial number of copies *in each dilution* (e.g., from step (a)) versus the cycle threshold.

The Examiner argued that Wittwer *et al.* described a method of "DNA monitoring at each PCR cycle by measuring melting curves and calculating copy number at each cycle." *See*, Office Action, page 4, second paragraph (underlining added). For this proposition, the Examiner cited five locations in Wittwer *et al.*: col. 3, lines 31-61, col. 4, lines 45-63, col. 7,

lines 14-31, Figures 22-23 and col. 17, lines 34-39. None of these locations describe determining a non-linear continuously differentiable function of a logarithm of copy number as a function of the cycle number at which the signal threshold value is exceeded. Indeed, note that the "determining" step does not involve copy number at each cycle as the Examiner suggests, but instead relies on the initial copy number of each dilution.

As figures often provide information in a way easier to understand than words, we address Figures 22-23 of Wittwer first. A review of the X and Y-axis labels of the Figures reveals that the graphs are of cycle number versus fluorescence, not a log of initial copy number as recited in the present claims. Each plotted line in Figures 22-23 is from one amplification reaction, whereas as discussed above, the "determining step" recited in the claims is based on determining a single function (i.e., a single line) representing multiple different amplification reactions having different starting copy number. While Figure 23 provides different plots based on different initial template copies, Figure 23 does not provide a single plot that provides a function of copy number and cycle number, nor does it suggest such a comparison. Thus, Figures 22-23 cannot and do not describe determination of a non-linear function involves plotting the logarithm of the initial number of copies in each dilution versus the cycle threshold.

Like the figures, the text of Wittwer *et al.* cited by the Examiner does not teach or suggest determination of a non-linear function involves plotting the logarithm of the initial number of copies versus the cycle threshold. There is no mention of such a step. Applicants acknowledge that some cited sections refer to the use of SYBR Green I, but it is not clear how this provides any useful information regarding the "determining" step.

The Examiner cited col. 4, lines 45-63 of Wittwer *et al.* as teaching a "correlation between the threshold cycle and the initial concentration of DNA templates [sic] copy number provides precise measurement of abundance of target nucleic acids and its non-linear functionality (3-dimensional spiral)." *See* Office Action, page 4, last paragraph. In fact, the reference to "3-dimensional" in the cited section of Wittwer *et al.* has nothing to do with non-linear equations. A full quotation of the paragraph follows:

> Furthermore, in contrast to measuring fluorescence once per cycle, embodiments of the present invention are disclosed which monitor

> **temperature**, **time** and **fluorescence** continuously throughout each cycle thus producing a 3-dimensional spiral. This 3-dimensional spiral can be reduced to temperature vs. time, fluorescence vs. time, and fluorescence vs. temperature plots. Fluorescence vs. temperature plots of the fluorescence from hybridization probes can be used to detect sequence alterations in the product. These sequence alterations may be natural, as in mutations or polymorphisms, or artificial, as in an engineered alternative template for quantitative PCR.
> (Emphasis added)

As highlighted above, the "three dimensions" referred to in the text are three variables in PCR that can be measured: temperature, time and fluorescence. There is not the slightest suggestion that "3-dimensional" refers to a non-linear equation.

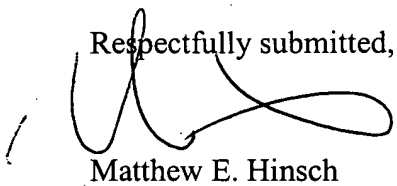
In view of the above remarks, Applicants submit that Wittwer *et al.* does not describe determination of a non-linear function involving plotting the logarithm of the initial number of copies versus the cycle threshold as the Examiner suggests. Therefore, Applicants respectfully request withdrawal of the rejection.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



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